Pneumonia in Chronic Kidney Disease patient: A Study of Clinical features and outcomes

By

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1. CAP: community acquired pneumonia
2. CKD: chronic kidney disease
3. DM: diabetes melitus
4. eGFR: estimated glomerular filtration rate
5. Non CKD: non chronic kidney disease
6. HDW: High Dependency Ward
7. ICU: Intensive Care Unit
8. LOS: Length of stay

ABSTRAK

Pneumonia dalam kalangan pesakit buah pinggang kronik: Kajian keatas ciri-ciri dan hasil klinikal

Latarbelakang: Pesakit buah pinggang kronik dikenalpasti sebagai satu kumpulan pesakit yang mudah mendapat pelbagai jangkitan dan mempunyai prognosis yang lemah. Namun begitu, tidak banyak kajian yang dijalankan ke atas kumpulan ini untuk menentukan ciri-ciri klinikal mereka dan memastikan hasil atau keputusan dari pneumonia.

Kaedah: Semua pesakit yang dimasukkan ke Hospital Universiti Sains Malaysia untuk penyakit komuniti pneumonia bermula dari Januari 2014 hingga Mei 2016 disaring kelayakannya untuk kajian ini. Nota kes subjek yang layak kemudiannya diekstrak daripada unit rekod dan dibuat semakan.

Keputusan: Sebanyak 398 rekod perubatan subjek diambil dari unit rekod dan dibahagikan pada nisbah 1:1 antara subjek pesakit buah pinggang kronik dan tidak kronik. Kami mendapati pesakit buah pinggang kronik adalah lebih tua (min umur 64 vs 56, dengan nilai P <0.05), mempunyai kadar morbiditi sama yang lebih tinggi, lebih ramai perokok dan tidak ramai divaksin. Mereka juga menunjukkan lebih berada dalam keadaan kejutan septisimia dan mempunyai status mental terubah (46%vs 23% P <0.05 dan 56% vs 26%, P<0.05), radiograf dada yang lebih teruk (54% vs 29%, P<0.05) dan skor PSI kumpulan yang lebih tinggi (52% vs 20%,P<0.05) berbanding pesakit lain yang bukan pesakit buah pinggang kronik. Kajian juga mendapati pesakit buah pinggang kronik mempunyai keputusan yang tidak memuaskan dengan

kadar mortaliti lebih tinggi (35% vs 12.7%, P<0.05), kadar kemasukan ke HDW/ICU lebih tinggi (50.2%vs 22%,P<0.05), median tempoh tinggal di hospital lebih lama (9 hari vs 6 hari,P<0.05) dan lebih ramai subjek yang memerlukan ventilasi mekanikal (37% vs 19.6%, P<0.005) .

Kesimpulan: Secara keseluruhannya kami menyimpulkan bahawa pesakit buah pinggang kronik mempunyai factor risiko yang tinggi yang boleh menyumbang kepada prognosis yang lemah. Namun begitu, kami mendapati kadar kematian untuk subjek kami melibatkan subjek yang mendapat komplikasi terutamanya mendapat jangkitan nosocomial.kami berpendpat dengan mengurangkan kadar jangkitan nosocomial maka kadar kematian dikalangan pesakit buah pinngang kronik yang mendapat jangkitan pneumonia

ABSTRACT

Background: Chronic kidney disease (CKD) patient is recognized as group of patient prone for various infection with poorer prognosis. However, not many studies have been done for this group of patient to determine their clinical features and to ascertain their outcomes in pneumonia.

Methods: All patients admitted for community acquired pneumonia from January 2014 to May 2016 in Hospital Universiti Sains Malaysia, Kubang Kerian Kelantan were screened for the eligibility to enroll in this study. Eligible subjects case notes were then extracted from the record office and reviewed.

Result: During the study period, a total of 398 subject's medical records were extracted from the record office, and were divided to 1:1 ratio between CKD and Non CKD subjects. CKD patient was noted significantly older (Mean age 64 vs 56, with P value <0.05), having more co morbidity, more smoker and less vaccinated. They did present as more in septicaemia shock and altered mental status (46% vs 23% P <0.05 and 56% vs 26%, P <0.05) with more severe chest radiograph (54% vs 29%, P <0.05) and more in high PSI score group (52% VS 20%, P <0.05) than were other patients without CKD. Patient with chronic kidney disease was also noted to have more unfavorable outcomes, higher mortality (35% vs 12.7%, P <0.05), higher HDW/ICU admission rate (50.2% vs 22%, P <0.05), longer median length of stay (LOS) (9 days VS 6 days, P <0.05), and

more subjects required mechanical ventilation (37% VS 19.6%, P <0.05) as compared to subjects without Chronic kidney disease.

Conclusion: We concluded that in overall picture CKD patient did come with higher prevalence with risk factor that can contribute to poorer prognosis. However, we did found that mortality in our subjects merely involved subjects that develop complication especially a nosocomial infection. This fact auspiciously provides us with a guide to further reduced mortality in CKD subjects with community acquired pneumonia.

1. INTRODUCTION

Chronic kidney disease (CKD) is fast emerging as a major public health problem (National Kidney Foundation 2002). Infection is common cause of morbidity and mortality in chronic kidney disease patient (Diego et al 2011). Although patients with CKD have an increased risk of bloodstream infection, urinary tract infection and pneumonia, little attention has been given to it and furthermore most of it is preventable (National kidney foundation 2002, James MT et al 2008, Naqvi SB and Collins AJ 2006).

When compared with the non-CKD population, the rates of pneumonia are 3 times greater in the CKD population and 5 times greater in the dialysis population (Naqvi SB and Collins AJ 2006). Despite being high risk and recognized as a special group, little is known in regard to its clinical presentation and outcome especially in Malaysian population.

Clinical presentation of the patient is of paramount importance to guide physician to initiate best line of treatment. As described clearly by Diego et al (2011) a CKD patient present differently for pneumonia. In this study Diego and his colleague pointed out that the majority of CKD population will come with severe pneumonia at presentation as compared to general population. It is not known however in this study if the patient have actually been presented earlier and treated with inappropriate treatment regime, i.e antimicrobial prior to admission. Thus it is of paramount importance to address this issue in regards to antibiotic usage and its limitation (due to impaired kidney function). As Malaysia have a different demographic background as compared to Diego et al study population, expanding knowledge regarding our own pneumonia pattern will definitely give an impact to current practice.

Diego et al also highlighted that prior pneumococcal vaccination did offer a protective factor for severe pneumonia especially in CKD population. Earlier meta analysis done by Anke Huss et al however indicated that vaccination was not an answer to prevent pneumonia even in high risk group such as CKD patient (Anke Huss et al 2009). Again, this issue was never investigated with regard to CKD patient in our community. Thus it is not known if our CKD patient was vaccinated and if vaccination affect prevention of pneumonia or severe pneumonia.

Streptoccoccus Pneumoniae was dominantly cultured in CKD patient as found out by Diego et al study. They also found out that there was no significant difference in CKD patient and non CKD patient with regards to etiology factor. This study did reveal however, that microbiology study was less performed in patient with CKD, a distinct clinical presentation was cited as the cause of this finding. With different presentation and clinical manifestation resulting with less favorable outcome (as portrayed by Diego et al), it is a compelling indication for further evaluation and research for this group of patient.

1.1 Pneumonia overview

1.1.1 Diagnosis of pneumonia

Pneumonia can be easily defined as infection of lung tissue. Some would more specifically define it as infection of lung parenchyma. However, as other disease, pneumonia also has had its own diagnostic criteria or diagnostic definition. A diagnostic criterion is important especially for the enrollment to the pneumonia clinical study.

Various recognizable society gave out their own definition and diagnostic criteria. The core of it however, seems to be coherent to each other. BTS (British Thoracic Society) defined a diagnosis of pneumonia as presence of acute lower respiratory tract symptoms and signs and can be confirmed by a positive chest x ray finding (NICE Pneumonia 2014).

A constellation of suggestive clinical features, and a demonstrable infiltrate by chest radiograph or any other radiological/imaging technique, with or without support by a positive microbiological cultures was suggested as diagnostic criteria for pneumonia by the Infectious Disease Society of America/ American Thoracic Society (IDSA/ATSC) Consensus guideline on management of community acquired pneumonia in adult (Mandel et al, 2007).

IDSA/ATSC and BTS diagnostic criteria share common similarities in term of suggestive clinical features and support by radiological evidence in diagnosing pneumonia. IDSA/ATSC however, adds on a positive microbiological culture as additional supporting evidence.

Chest radiograph is an important supporting evidence of pneumonia diagnosis in both NICE 2014 guideline as well as in IDSA/ATSC guideline. Typical chest radiograph finding in community acquired pneumonia range from lobar consolidation, interstitial infiltrate, and/or consolidation. However, evidence suggests that there is no significant difference in radiological finding between bacterial etiology versus non bacterial etiology in pneumonia patient (Marie TJ, 1994). Furthermore, there is also potentially substantial interobserver variation between

radiologists as well as between emergency physician and radiologist as pointed out in several studies (Hopstaken et al 2004, Albaum et al 1996, Campbell et al 2005). Hence, a more accurate radiological investigation such as high resonance CT scan is needed to confirm the diagnosis in certain cases (Claessens et al 2015).

In summary, a diagnosis of pneumonia can be made based on suggestive clinical symptoms and supported by a chest radiograph with typical pneumonia features and can be further reinforced by a positive microbiological culture. A HRCT scan has proven more superior than chest radiograph to detect a pneumonia lesion (Claessens et al 2015).

1.1.2 Incidence of pneumonia

Worldwide estimation of pneumonia burden involved approximately 450 million people annually. In UK, incidence rate was estimated at around 6 cases per 1000 population age 18-39 year old, and the figure increase to 75 cases per 1000 population in 75 year old population group (Hoare Z and Lim WS 2009).Chou CY et al found that estimated incidence of pneumonia among CKD patient was 65.6 per 1000 person-years, whereas Non CKD person the incidence was 28.4 per 1000 person-years.

Chronic kidney disease group patient is known to have an increased risk of infection, with pneumonia being one of it. It was also postulated that this group of patient had poorer prognosis as compared to general population (Naqvi SB and Collins AJ 2006, Slinin Y, Foley RN and Collins AJ 2006).

1.1.3 Clinical features of pneumonia

Majority of previous studies concentrated more on management of pneumonia, rather than identifying more accurate symptoms and signs of pneumonia. NICE 2014 elaborated in detail with regard to clinical signs and symptoms of pneumonia. It defined pneumonia as an infection of lung tissue, diagnosed based on signs and symptoms of an acute lower respiratory tract infection. Cough is usually the main symptom, accompanied with at least one other symptom such as fever, sputum production, breathlessness, wheezing or chest discomfort or pain without any other explainable cause. This list is not unfamiliar to our medical fraternity, consistent with the high frequency of pneumonia diagnosis.

Unfortunately, systemic review of clinical symptoms such cough, and clinical sign such as fever, tachycardia and typical lung finding of crackles only offer a sensitivity of less than 50% even after using chest radiograph findings as standard investigation (Metlay JP and Fine MJ, 2003), making the diagnosis of pneumonia difficult. Daily clinical rounds however, usually lead by progressive clinical evidence, enabling other clinical possibility to be treated simultaneously or being considered as soon as new and contrary evidence is eminent. Various earlier studies explored further in regards to clinical features of community acquired pneumonia (CAP). Metlay and his friend, Fine had another review done earlier in 1997, reviewing various article associated with community acquired pneumonia to determine what clinical features and history can predict likelihood of CAP. In this article Matley and his colleague finally concluded that no constellation of historical and physical findings should be able to diagnose pneumonia accurately. However,

they did find in their review that a diagnosis of CAP is less likely in the absence of vital sign abnormality and lung physical findings such as crackles (Metlay et al, 1997). Elderly patient require more careful evaluation as they may present differently and atypically. Various articles have suggested screening patient with probable pneumonia with pulse oximetry to detect hypoxaemia to be essential especially in people with atypical presentation (Fine MJ et al 1997, Mover WR et al 1995, Levin KP et al 2001)

A set of clinical features has been used as severity parameters in the current standard practice. CURB 65 and Pneumonia Severity Index (PSI) is the two most popular calculators to determine the severity of pneumonia. Thus, all the clinical features listed in both list are important and significant clinical features of pneumonia. CURB 65 comprised of a Conscious level (C) – based on the assessment of mental state orientation towards place, person and time. U was designated for assessment of urea. A level more than 7.0 mmol/L would be considered as abnormal result. Another important parameter in this scoring system is respiratory rate. An abnormal result is defined with a respiratory rate of 30 and above. The B stands for abnormal blood pressure. A systolic level of 90 and below and a diastolic level of 60mmHg and below is considered as abnormal. Lastly this scoring system also consider age factor as an important risk factor.

Pneumonia Severity index (PSI) has been also been widely used by medical practitioners to grade the severity of pneumonia. PSI is a more comprehensive and detailed tool with 20 variables. Among the clinical features listed in PSI is presence of altered mental status, low blood pressure, tachycardia, tachypnoea and abnormal body temperature. Aujesky considered all

these clinical features merely important features for prognostication rather than diagnosing (Aujesky D et al 2005).

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1.1.4 Etiology of pneumonia

IDSA/ATSC strongly advised for etiologic directed therapy in pneumonia. It is more fundamental especially in severe pneumonia. However, no similar strong recommendation has been made for patient with community acquired pneumonia treated as outpatient. This is because various evidence showed that culture and sensitivity test to determine etiology in this group of patient is rarely done. However, they seems to respond well on current empirical antibiotic usage (Malcom C and marrie TJ 2003, Fine MJ et al 1997)

Appropriate test is important in order to detect or to determine an appropriate etiology of pneumonia. Various studies have reviewed the effectiveness of selected clinical laboratory test for this job. IDSA/ATSC suggested that pre treatment blood culture and sensitivity would give a positive yield between 5-14%. This figure was based on its review on multiple articles (Mandell et al 2007). IDSA/ATSC also highlighted the importance of taking blood culture prior to initiation of antibiotic. It is known that blood culture and sensitivity yield is reduced to half with prior antibiotic therapy (Metersky ML et al 2004). Blood culture was assigned as optional in majority of CAP cases. IDSA/ATSC only emphasized the importance of this test in several selected cases such as severe pneumonia and patient with multiple risk factors for bacteremia.

Sputum culture is one of the common investigations done for CAP patient. However, it has been highlighted as giving out a low yield by IDSA/ATSC consensus. It also known that high PSI does not contribute to high yield in sputum culture as blood culture does. The main setback for sputum culture is in producing satisfactory sample, as it is affected by transportation issues as well as quality of the entire sample processing step.

Other culture commonly done for CAP patient is pleural fluid culture. Although has been tagged as a low yield by IDSA/ATSC; it has a significant impact on management decision for either antibiotic usage or indication of drainage.

Antigen test is another test frequently performed in CAP patient. Of the various antigen tests available, the legionalle urinary antigen test offer good alternatives to culture tests, especially when culture sample is difficult to obtain or unable to give a good yield.

Overall etiology of pneumonia is determined by various factors. According to Daniel and Anna, pre vaccine era bugs, streptococcus pneumonie remained the dominant organism in CAP patient. His prevalence however was significantly reduced from 95% in those era to current situation of 10 -15% (Daniel and Anna 2014). The dominant organisms found in CAP patient would be *S. Pneumonie, K. pneumonie, mycoplasma and hemophilus influanzae*. IDSA/ATSC highlighted slight differences in term of dominant organism in non ICU versus ICU patients. They found that

S. aureus organism was also common in patients treated in ICU. Etiologies of pneumonia in CKD patient versus non CKD remain the same with almost similar pattern in Diego et al study.

1.1.5 Outcomes of pneumonia

Mortality for inpatient CAP patient is about 10-12% (Daniel and Anna 2014, Fine MJ et al 1997). Diego et al 2011 found that there is an increase in overall mortality in CKD patient. However he also found that there no significant difference in term of ICU admission and need for mechanical ventilation (Diego et al 2011)

Health care associated pneumonia or HCAP is a different entity that postulated having different outcome and clinical entity. It is advisable that this group of patient to be differentiated with the current group of CAP (Kollef MH 2005). However, recent studies suggest that HCAP concept does not accurately identify resistant organisms and its high mortality not merely because of higher frequency of resistant organisms (Chalmers JD et al 2014, Gross AE et al 2014, and Yap V et al 2013).

Outcome of pneumonia can be affected by various factors, various studies was done to address this issue. CURB 65 and PSI assessment as discussed earlier can be used for prediction of pneumonia severity as well as its prognosis and mortality prediction.

Beyond these two scoring systems, a retrospective analysis was done by Metersky ML with a database of more than 21000 patients. Seven factors were identified to be significantly associated with mortality prior to discharge. The seven factors were; a systolic blood pressure of less than 90 mmHg, respiratory rate more than 30 breaths per minutes, presence of bacteriemia, arterial PH less than 7.35, blood urea more than 11 mmmol/L, arterial partial oxygen concentration less than 60mmHg or saturation of oxygen <90% and lastly the need for mechanical ventilation (Metersky ML et al 2012). Even though most of the factors have already been listed in CURB 65 as well as in PSI scoring system, this study further emphasized important factors that can contribute to pneumonia severity as well as prognosis and outcome.

Prognosis and outcomes also can be affected in the group of patient called 'non responding' patient. Menendez R quantified this group of pneumonia patients as those who were not responding to empirical antibiotic treatment within the first 72 hour. His study was able to identify 15.1% of their subjects as non responder. Those with liver disease, high pneumonia risk class, leucopenia, severe radiograph features such as multilobar, pleural effusion and cavitation were identified as independent risk factors for the non responder. Mortality can be as high as 25% in the non responder group (Menendez R et al 2004)

1.2 Overview of Chronic Kidney Disease

International society of nephrology via its KDIGO 2012 clinical practice guideline for evaluation and management of chronic kidney disease(CKD) defined CKD as abnormalities of kidney structure or function, present for more than 3 months duration with implication to health. They further explained that CKD criteria can be either presence of any marker of chronic kidney disease such as presence of significant albuminuria, urine sediment abnormalities, histological abnormalities, history of renal transplant, structural abnormalities noted by imaging modalities, electrolyte abnormalities caused by tubular disorder or presence of decreased glomerular filtration rate (GFR) of less than 60ml/min/1.73m^2 (International Society Of Nephrology (ISN) 2012)

Definition of GFR of less than 60ml/min/1.73m^2 was suggested by KDIGO guideline which represented less than half of normal value in normal adult man and women (International Society of Nephrology 2012). This estimated calculation was based on various hallmark studies as early as Rowe JW et al in early 1976 and further supported by latest study done by Rule AD et al and Poggio et al in year 2010 and 2009 respectively.

Various evidences pointed out that a GFR less than 60ml/min/1.73m^2 is associated with higher risk of complication when compared to subjects with GFR more than the above figure. Among the most popular was a Meta analysis done by Matshusita K et al 2010. This Metaanalysis showed an association of eGFR less than 60ml/min/1.73m^2 with cardiovascular mortality, kidney failure and risk of CKD progression (Matshusita et al 2010).

KDIGO also suggested current routine laboratory testing to estimate GFR (eGFR) using serum creatinine as one of the marker was sensitive enough to detect GFR of 60ml.min/1.73m^2. They also postulated that at this level of GFR subjects are more prone to other complication such as drug toxicity, metabolic and endocrine complication (International Society of Nephrology 2012).

KDIGO guidelines further classified CKD into a few categories. Chronic kidney disease is commonly divided into stages based on either eGFR or its albuminuria level. Staging based on estimated glomerular filtration rate are the most frequently used in clinical practice. Matsushita et al 2012 study found that both albuminuria level as well as estimated glomerular filtration rate was equivalent in estimating adverse implication to health.

Stages of chronic kidney disease based on estimated glomerular filtration rate were divided into 5 stages (Table 1.1). 1st stage or level known as G1 stage is defined as estimated glomerular filtration rate of more than 90ml/min/1.73m^2 and is described as normal or high kidney function. Second stage is for estimated glomerular filtration rate between 60- 89ml/min/1.73m^2, and is described as having mildly decreased renal function. Both stage were not considered to fulfill the chronic kidney disease definition unless they have other evidence of kidney damage. The chronic kidney disease stages continue with stage G3a whereby its estimated glomerular filtration rate ranged from 45 to 59ml/min/1.73m^2. This stage is illustrated as having mildly to moderately impaired kidney function. G3b stage have an estimated glomerular filtration rate of 30 – 44ml/min/1.73m^2. This stage is further described as having moderate to severe kidney function

impairment. Stage G4 with estimated glomerular filtration rate of 15 – 29ml/min/1.73m^2, is categorized as having severely decreased renal function. Lastly grade G5 with estimated filtration rate of 0 – 14ml/min/1.73m^2. This group is classified as having renal failure.

Chronic kidney disease based on degree of albuminuria was divided into three different stages (Table 1.2). They divided the category into 3 parts, 1st category A1has albuminuria excretion rate of less than 3mg/mmol. This category is described as having normal to mildly impaired renal function. Category A2, with albumin excretion rate of 3 – 30mg/mmol albuminuria, subjects with moderately impaired renal function is classified into this category. A3 category has albumin excretion rate more than 30mg/mmol. A subject in this category is considered as having severe impaired renal function. KDIGO also allowed usage of protein reagen strip test to replace albumin excretion rate if it was not available. Negative or trace protein reagent strip test was put in A1 category, A2 as having 1+ and A3 with more than 1+ protein reagent strip test result. Albuminuria has been shown by various studies to be less sensitive as compared to glomerular filtration rate (Yasmin A and Hasniza ZH 2015).

GFR Category	GFR (ml/min/1.73)	Terms
G1	>/= 90	Normal or High
G2	60 – 89	Mildly decreased
G3a	45 – 59	Mildly to moderately decreased
G3b	30 – 44	Moderately to severely decreased
G4	15 – 29	Severely decreased
G5	<15	Kidney failure

TABLE 1.1: Stages of CKD based on GFR (extracted from KDIGO Clinic practice guideline for evaluation and management of CKD 2012)

Category	AER (mg/24 hrs)	ACR (approximate equivalent)		Terms
		(mg/mmol)	(mg/g)	
A1	<30	<3	<30	Normal to mildly decreased
A2	30 – 300	3-30	30 - 300	Moderately increased
A3	>300	>30	>300	Severely increased

Table 1.2: Stages of CKD based on albuminuria. (extracted from KDIGO Clinic practice guideline for evaluation and management of CKD 2012)

1.3 Multiple etiologic factors can contribute to development of chronic kidney disease.

A study done recently in Hospital University Sains Malaysia (HUSM) by Mohamed Salman et al 2015 in collaboration with HUSM chronic kidney disease resource center found that majority of subjects in their study have their cause of chronic kidney disease as secondary to diabetic nephropathy (44.9%). Hypertensive kidney disease was the second commonest cause in their cohort with 24.2% or two hundred and two subjects. Others causes of chronic kidney disease were obstructive uropathy (9.2%), glomerulonephritis (6.2%), toxic nephropathy 2.1%, and adult polycyctic kidney disease (2.2%). Miscellaneous cause was 0.8% and eighty subject (9.4%) had unknown cause.

The incidence of chronic kidney disease is increasing over the past years. A study done by Hooi LS et al 201 to determine the prevalence of chronic kidney disease among Malaysia adult found out that the prevalence of chronic kidney disease was 9.07%, with 4.16% were in CKD stage 1, 2.05% stage 2, 2.26% stage 3, 0.24% in stage 4 and 0.36% stage 5. Hooi study finding was noted to be contrary with another study done by Mohamed Salman et al (2015). Mohamed Salman and his colleague noted increasing in trend of CKD prevalence among their study subjects. 2.1% in chronic kidney disease stage II, IIIa (8.7%), stage IIIb (21.9%), stage IV (28.1%) and three hundred thirty three subjects or 39% were CKD stage V. However it is understandable that this two studies to have two different findings as the 1st study done by Hooi and his colleague were done with normal healthy adult population whereas Mohamed Salman study used subjects extracted from patient admitted to hospital for the past 5 years.

Multiple studies call attention to that CKD subjects having increased risk with all cause of mortality and all type of infections (Diego et al 2011, Naqvi SB and Collin AJ 2006, Matshusita et al 2012, Dalyrample LS et al 2012, James MT et al 2009, Wu MY et al 2012). However, upon reviewing all this articles there are a few unresolved questions. Among others were how did they CKD subjects get medical attention, how well they responded to our standard treatment and last but not least was there an indication for us to treat them in a different way empirically (of course with good evidence based on common etiologies among their group).

1.4 Pneumonia in Chronic Kidney Disease patient

Christian and his colleagues proposed few mechanisms that can contribute to lower immunity among patient with CKD (2013). A chronic kidney disease directly has several consequences to human body. The author Christian and his colleague invented a diagram which can explain thoroughly this postulated theory (see figure 1.1).

From this article and diagram, the authors suggest few mechanisms that chronic renal failure can lower down human immune system. Immunosuppresion occur via uraemic accumulation of toxic metabolic waste, the increased turnover of the components of the alternative complement pathway because of impaired protein catabolism, and in cases of extensive proteinuria, the urinary loss of proteins with immunological functions (Christian et al 2013).

In reality, as suggested from various studies namely, Naqvi and Collin AJ (2006), Diego et al 2011, Antoni T et al 2013 and few others that a CKD state pose a reasonably higher risk for developing pneumonia. However, only some of this handful studies did highlight even the outcomes of pneumonia are worse than normal population. Diego et al 2011 among others highlighted that pneumonia in CKD population carries poorer outcome. Marin HK review a large US database for culture positive pneumonia also conquer with the finding. In this study, author found that among others, high urea and creatinine are an independent risk factor for mortality in pneumonia (2005).

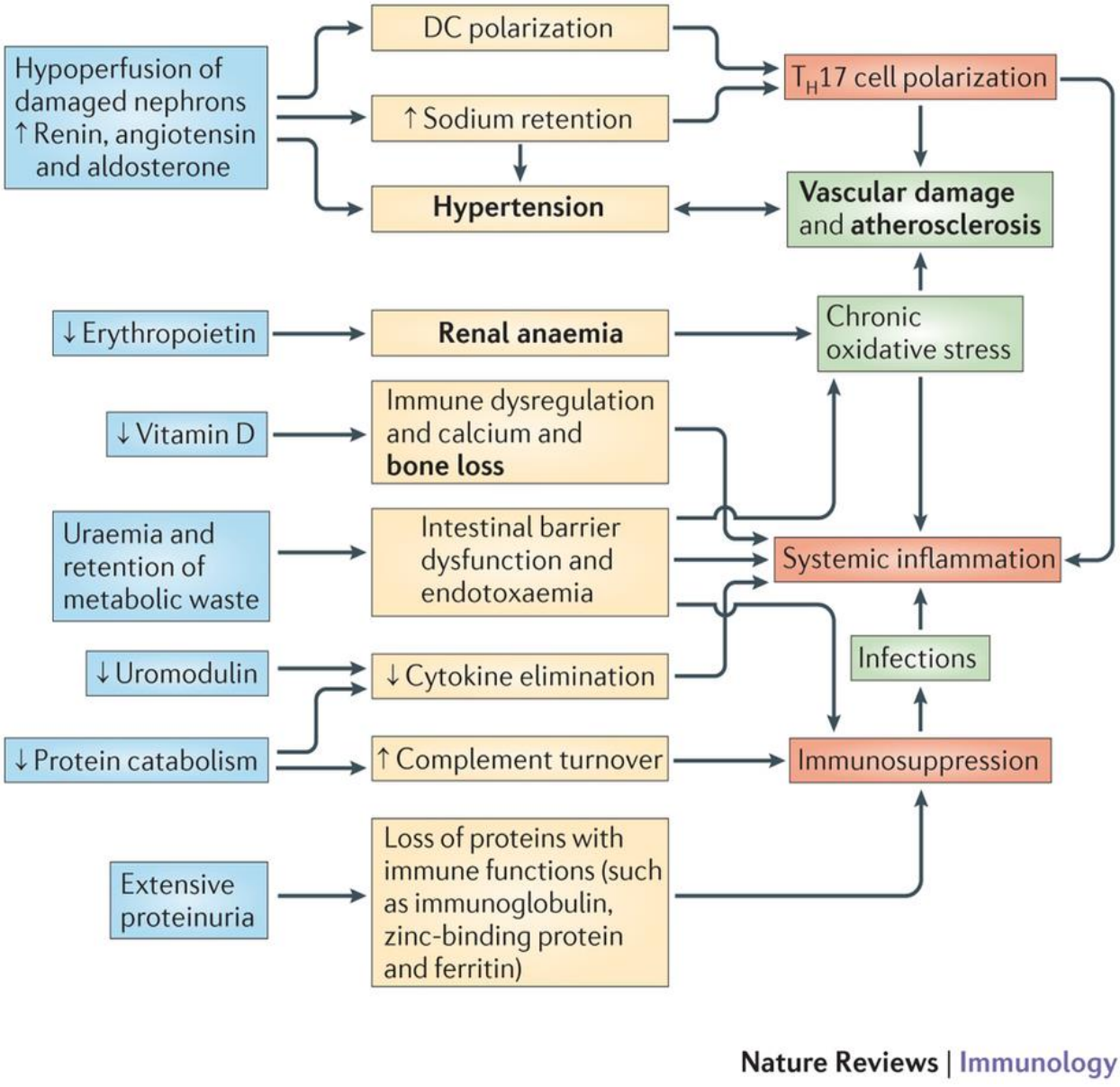

Figure 1.1: Proposed mechanisms that effect immunity among CKD patient. Extracted from Christian K et al 2013.

1 OBJECTIVE

3.1 GENERAL

To study the clinical features, outcomes and associated factors in CKD and Non CKD patients affected by community acquired pneumonia

3.2 SPECIFIC

1. To determine main clinical features of community acquired pneumonia (CAP) that required hospitalization among Chronic Kidney Disease (CKD) patient, in comparison with non CKD patient.
2. To determine length of hospital stay (LOS), ICU admissions, need for mechanical ventilation and mortality among CAP patient with CKD in comparison with patient without CKD.
3. To determine the causative organism for CAP among patient with CKD in comparison with patient without CKD.

3.3 RESEARCH QUESTION

What are the clinical features and outcomes, clinical features and etiological agents among in patient chronic kidney disease (CKD) patient?

3.4 HYPOTHESIS

There is significance difference in presenting clinical features of CAP such as presence of fever, cough, abnormal conscious level, tachypnoea, tachycardia and hypoxia between chronic kidney disease (CKD) group and Non chronic kidney disease group

There is significance difference in presenting laboratory/radiological features of CAP such as baseline hemoglobin level, total white blood cells, albumin level, chest radiograph severity and total PSI score between CKD and Non CKD patient

There is significance difference in outcomes of CAP patient such as length of hospital stay (LOS), mortality, requirement of mechanical ventilation, and ICU/HDW admission rate between CKD and Non CKD group

There is significance different in causative organisms of CAP in CKD patient comparing to Non CKD patient.

4. METHODOLOGY

4.1 Study Design

Retrospective record review.

4.2 Study approval

This study was approved by the Research and Ethic Committee, Universiti Sains Malaysia.

Approval reference code: USM/JEPeM/16020068

4.3 Study period

We conducted a retrospective review of medical records of the patient that had been admitted with a diagnosis of pneumonia from 2014 through May 2016 to Tertiary Teaching Hospital; Hospital Universiti Sains Malaysia.

4.4 Study population and setting

Admission registry from admission book in all medical wards and Intensive care Unit in Hospital Sains Malaysia (HUSM) has been reviewed. Patient admitted with diagnosis of Community acquired pneumonia from January 2014 till Apr 2016 then identified.

Medical records of the eligible subjects then traced from record office using patient's registration number (RN). Only Community acquired pneumonia cases with complete clinical data, medical record and fulfilled all inclusion criteria without any exclusion criteria were recruited in the study. Potential subjects then divided into two group based on their previous known kidney function status. Chronic Kidney Disease group consists of subjects that fulfil definition of having underlying Chronic Kidney disease as has been delineated in the operational definition section. Subjects without Chronic kidney disease were in the other group.

Data then extracted from subjects medical records, online HUSM radiology system and microbiology lab records. Outcomes were recorded till patient has been discharge home.

4.5 Data collection

The subjects for this study was identified from wards registry and the intended data was collected from subjects medical records, online Hospital Sains Malaysia radiology system as well as microbiology laboratory lab registry and records.

Subjects demographic data such as age, sex, smoking habit, race, vaccination history together with history of underlying co morbid and prior (pre admission) antibiotic usage was extracted from subject medical records.

Subjects clinical features at admission was obtained either from admission notes from casualty department or referral letter notes from other hospital/clinic if the subject was a referred case from other hospital/clinic. Fever and cough duration history, screening saturation oxygen, vital sign reading mainly blood pressure and heart rate, respiratory rates and concious level by using Glascow Coma Scale (GCS) asessment were the clinical features variables that has been extracted.

Laboratory variables obtained primarily from medical report, supported by Hospital Sains Malaysia online pathology or radiology report system as well as laboratory records and registry. Variable such as full blood count, renal profiles, arterial blood gases, glucose level, albumin level (corrected) and chest radiograph was obtained and documented. Microbiology report was obtained from documentation in medical report and microbiology laboratory registry and reports.

Subjects progress in ward then reviewed and documented. Variable such as subjects antibiotic regime used in ward, ICU/HDW admission, mechanical ventilation, length of hospital stay outcome and progress is well obtained. Cause of death was also obtained from copy of death certificate available in the subjects medical record.

4.6 Sampling method

Two thousand four hundred and eighty seven community acquired pneumonia patients admitted was obtained from medical report reviewed. From this number; only two thousand one hundred and fourteen patients had their records available. This analysis was done via online medical records registry system. The other three hundred and seventy three patient records were not available due to various reason, among others was a wrong registration number entered in the admission registry, or human error while copying the patient registration number from admission registry booklet.

Inclusion criteria was then applied to remaining subjects. Only one thousand five hundreds and two subjects was subsequently selected. 1502 subjects then further divided into 2 group based on their renal function. 1108 subjects belong to non Chronic kidney diasease (non CKD) group and the later 394 subjects were in the chronic kidney disease (CKD) group.

A 199 subjects were further extracted from both group via simple random sampling method. Each potential subjects from study population in each group were randomly selected by using their registration number via a lottery method. Medical records for this 199 subjects in each group then been traced and its datas were extracted, examined and documented.

Extra precaution taken if subject do not have their previous renal function readily available; i.e from previous medical records or from referral notes if patient from other hospital/clinic. No subjects were put into CKD group without evidence that they had underlying abnormal renal function for 3 months duration as per CKD definition. In view of objective of this study mainly to observed effect of chronic kidney disease to community acquired pneumonia patient, all patients with evidence of acute kidney injury and acute on chronic renal disease were excluded from study.

4.7 INCLUSION AND EXCLUSION CRITERIAS:

Inclusion criteria:

1. Patient with clinical or/and radiological diagnosis of community acquired pneumonia.
2. Age more than 18 year old (>18 years old)
3. Baseline renal function that can fulfilled criteria of CKD or Non CKD

Exclusion criteria:

1. Patient admitted with diagnosis of hospital acquired pneumonia. Patient with hospital acquired infection has higher mortality and morbidity, not included in this study.
2. Patient known in immunodeficiency state such as HIV, or on prophylaxis antibiotic post removal of spleen, Patient who had rheumatological or hematological disorder and/or currently on immunosupressive drug or long term steroid usage.